

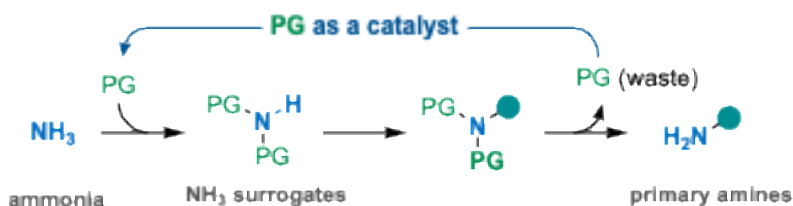
Catalytic Direct Synthesis of Primary Amines from Ammonium Salts: Protecting Groups as Catalysts

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Primary amines are indispensable building blocks in pharmaceuticals, agrochemicals, and functional materials, yet their direct catalytic synthesis from ammonia remains difficult owing to over-alkylation and catalyst poisoning. We therefore exploited ammonia and its bench-stable forms, ammonium salts, as practical nitrogen sources for direct primary amine synthesis. Previously, we developed the direct amination of allylic alcohols with aqueous ammonia using a Pt/DPEphos catalyst, affording primary allylamines with high monoallylation selectivity and water as the sole by-product.¹ A more practical Pd-catalyzed variant then used ammonium acetate as both a nitrogen source and a Brønsted acid, enabling the reaction under mild, pressure-free conditions in a simple vial with ready scalability.²

Building on these results, we developed a carbonyl catalysis strategy in which a protecting group itself functions as a catalyst. Diaryl ketones, conventionally used to protect ammonia as N–H ketimines, integrate protection, N–H functionalization, and hydrolytic deprotection into a single catalytic cycle. As a proof of concept, amino-trifluoromethylation of alkenes with ammonium formate and the Togni reagent, catalyzed by a rationally designed diaryl ketone catalyst, afforded a broad range of β -trifluoromethylated primary amines, including α -tertiary amines and derivatives of complex natural products.³ The reaction runs in a standard flask (~ 1 atm), is amenable to gram-scale and ^{15}N -labeled synthesis, and delivers a bioactive building block in a single step (44%) that previously required four steps (4% overall). Together, these studies establish ammonium salts as practical nitrogen sources, and carbonyl catalysis as a versatile platform for the direct, modular synthesis of structurally diverse primary amines.



References: (1) Das, K.; Shibuya, R.; Nakahara, Y.; Germain, N.; Ohshima, T.; Mashima, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 150. (2) Kataoka, S.; Morimoto, H.; Ohshima, T. *J. Org. Chem.* **2024**, *89*, 10693. (3) Shimozono, K.; Nishimoto, N.; Tagami, T.; Ohshima, T. *submitted*.